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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/147,919 | 03/23/1999 | MARY JANE CARDOSA | 20239-703 | 2431 |

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| EXAMINER | |
|---|---|
| MOSHER, MARY | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1648 | 11 |

DATE MAILED: 11/30/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/147,919 | Cardosa et al |
| **Examiner** | **Art Unit** |
| Mary Mosher | 1648 |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on *9/20/01* .

2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under ***Ex parte Quayle***, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) *15-38* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☒ Claim(s) *27, 28, and 32* is/are allowed.

6) ☒ Claim(s) *15-26, 29-31, and 33-38* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

## DETAILED ACTION

### *Claim Rejections - 35 USC § 112*

Claims 29-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record. Applicant again argues that the specification teaches methods of administering the two component composition to an animal and teaches the timing of administration of the two components, and argues that the specification teaches how to optimize co-expression of the two components by using the same inoculation site for both components. Applicant asserts that nearly all cells close to the injection site will contain the vector encoding the dengue epitopes, resulting in cells recombinant for both components. Applicant is requested to point to evidence supporting this assertion, as the examiner is not aware of any evidence of a high transformation rate for the entire area of an injection site for DNA administered in vivo, nor high reproducibility in contacting the exact same cells with a needle in multiple injections. Note that MVA does not spread from cell-to-cell in mammals; neither do most DNA vectors. Therefore, in the absence of evidence of success, one skilled in the art would have reason to doubt that administration of separate T7-controlled DNA vector and T7-polymerase-encoding MVA by conventional methods, such as injection, would lead to uptake of both components by the same cells and expression of the encoded products in amounts sufficient to induce an immune response. Applicant asserts that only routine optimization is required. Considering the unpredictability of

inducing an immune response, the absence of any prior art teaching how to administer similar 2-component expression systems to an intact subject (as distinct from administering 2-component expression systems in isolated cultured cells), the limited guidance in the specification, and the absence of working examples, it is maintained that more than routine optimization is require to practice the method as claimed.

***Claim Rejections - 35 USC § 103***

Claims 15-17, 19-26, 35 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Sutter et al (C2) or Altenburger (US 5,185,146), in view of Lai et al (US 5,494,671), and further in view of either Monath et al (Fields Virology) or Kelly et al (US 6,074,865), and any of Moss or Paoletti et al (WO 92/15672) or Nazerian et al (US 5,369,025), for reasons of record. New claims 35 and 36 have been added to this rejection, because Lai et al teaches expression of dengue E antigen. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicant argues that Sutter, Altenburger, and Lai do not teach multiple dengue serotypes, and that Monath teaches only live attenuated complete dengue viruses. However, Monath provides motivation for including multiple dengue serotypes simultaneously "in order to avoid sensitizing the vaccinee to more serious disease", and Lai provides motivation to express a specific Dengue subunit. Applicant argues that Kelly does not teach or suggest that at least one antigen from two

or more serotypes results in immunity to all four serotypes. However, Kelly explicitly suggests using a tetravalent vaccine containing antigens of all four serotypes in a vaccine "to provide protection against dengue disease." Paoletti and Nazerian both teach or suggest a poxvirus, analogous to the claimed MVA poxvirus, which expresses antigens for multiple serotypes of a viral pathogen, analogous to the claimed dengue pathogen. It is maintained that, in view of the combined teachings of the references, the invention as a whole is obvious, absent unexpected results.

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over either Sutter et al (C2) or Altenburger (US 5,185,146), in view of Lai et al (US 5,494,671), and either Monath et al (Fields Virology) or Kelly et al (US 6,074,865), and any of Moss or Paoletti et al (WO 92/15672) or Nazerian et al (US 5,369,025), as applied to claims 15-17 and 19-26 above, and further in view of Sutter et al (PNAS 89:10847-10851, 1992), for reasons of record. Applicant's arguments involving the separate teachings of the references are addressed above.

New claims 33-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Sutter et al (C2) or Altenburger (US 5,185,146), in view of Paoletti et al (5,744,141 and 5,514,375) and either Monath et al (Fields Virology) or Kelly et al (US 6,074,865), and any of Moss or Paoletti et al (WO 92/15672) or Nazerian et al (US 5,369,025). This rejection is similar to the rejection of record for claims 15-17, 19-26, but Lai et al is replaced with two patents of Paoletti et al. These claims differ from the above claims in that separate claims specify preM antigen, E antigen, or NS-1 antigen, for two to four of the four dengue serotypes. Unlike Lai et

al, Paoletti teaches a recombinant vaccinia comprising the entire preM, E, and NS-1 dengue coding sequences, see Example 13 in each patent. 5,514,375 contains a figure illustrating the dengue regions in each construct, see figure 19; 5,744,141 contains the results of immunization tests using the constructs, see Table 12. As discussed previously, Sutter and Altenburger teach MVA as a useful vaccinia vaccine vector, Monath and Kelly suggest simultaneous vaccination against all four serotypes of dengue, and Moss, Paoletti (WO) and Nazerian all teach using vaccinia or other poxvirus as a polyvalent vaccine. It would have been within the ordinary skill of the art to combine the dengue coding region of Paoletti et al with the MVA strain of vaccinia to obtain the advantages of MVA taught by Sutter and Altenburger; it would further have been within the ordinary skill of the art to use the same coding region from all four dengue serotypes to achieve the tetravalent vaccine suggested by Monath and Kelly, and to use a single vaccinia construct for a multivalent vaccine as suggested by Moss, Paoletti (WO), and Nazerian. The invention as a whole is therefore prima facie obvious, absent unexpected results.

### *Allowable Subject Matter*

Claims 27, 28, and 32 are allowed, for reasons of record.

### *Conclusion*

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is (703) 308-2926. The examiner can normally be reached on Monday -Thursday and alternate Fridays from 6:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this Group is now (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

November 29, 2001

MARY E. MOSHER
PRIMARY EXAMINER
GROUP ~~1800~~ 1600